Elevate Series

ANNALS OF MEDICINE
2025, VOL. 57, NO. 1, 2442065
https://doi.org/10.1080/07853890.2024.2442065

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Risk factors for severe postpartum hemorrhage in placenta accreta spectrum patients undergoing prophylactic resuscitative endovascular balloon occlusion of the aorta during cesarean delivery

Xiafei Wu[a,b*], Jie He[a,b*], Yuxiang Bai[a,b], Yanqiong Gan[a,b,c], Hongbing Xu[a,b], Hongbo Qi[a,b,d**] and Xinyang Yu[a,b**]

[a]Department of Obstetrics, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China; [b]Chongqing Key Laboratory of Maternal and Fetal Medicine, Chongqing Medical University, Chongqing, China; [c]Department of Obstetrics and Gynecology, Affiliated Hospital of North Sichuan Medical College, Nanchong, China; [d]Department of Obstetrics and Gynecology, Women and Children's Hospital of Chongqing Medical University, Chongqing, China

ABSTRACT

Objective: This study aims to investigate the risk factors for severe postpartum hemorrhage (SPPH) in patients with placenta accreta spectrum (PAS) undergoing cesarean delivery, despite the prophylactic use of resuscitative endovascular balloon occlusion of the aorta (REBOA).

Materials and methods: We conducted a retrospective case–control study on PAS patients who underwent cesarean delivery with prophylactic REBOA at the First Affiliated Hospital of Chongqing Medical University from January 2017 to December 2021. Prophylactic REBOA placement was determined by a prenatal ultrasound scoring system. Patients were divided into those who experienced SPPH (case group) and those who did not (control group), with SPPH defined by one or a combination of the following criteria: intraoperative blood loss ≥1500 mL, transfusion of ≥4 units of packed red blood cells, intraoperative hysterectomy, or sequential uterine artery embolization. Propensity score matching (PSM) was employed to minimize biases, and multivariate logistic regression was used to calculate adjusted odds ratios (aOR) for risk factors.

Results: Of the 424 enrolled patients, 102 experienced SPPH (case group), while 322 did not (control group). After PSM, the case group comprised 79 patients, and the control group included 130. After adjusting for confounders, patients with placenta increta (aOR 3, 95% CI 1.49–6.03, $p=0.002$), percreta (aOR 21.77, 95% CI 6.57–72.09, $p<0.001$), lower hemoglobin levels (aOR 0.98, 95% CI 0.95–1, $p=0.050$), and higher D-dimer levels (aOR 1.36, 95% CI 1.12–1.65, $p=0.002$) had an elevated risk of SPPH. Threshold effect analysis indicated no significant nonlinear relationship between hemoglobin, D-dimer, and outcomes.

Conclusions: PAS patients, particularly those with placenta increta and percreta, lower hemoglobin levels, and elevated D-dimer levels, are at an increased risk of SPPH during cesarean delivery, even with REBOA intervention.

KEY MESSAGES

- PAS patients are more likely to experience hemorrhage during cesarean deliveries.
- REBOA is effective for managing intraoperative bleeding, yet a subset still experiences SPPH.
- Our study identifies several risk factors in PAS patients who experience SPPH despite REBOA intervention.

ARTICLE HISTORY

Received 8 August 2023
Revised 27 March 2024
Accepted 14 November 2024

KEYWORDS

Aorta; abdominal; balloon occlusion; placenta accreta; postpartum hemorrhage

Introduction

Placenta accreta spectrum (PAS) disorders refer to heterogeneous conditions characterized by abnormal adhesion and invasion of the placental trophoblast into the myometrium and, in some cases, the uterine serosa [1]. The incidence of PAS has been increasing considerably in the past decades from approximately 0.005% to 0.01%–1.1% [2,3]. A 2021 study based on a U.S. inpatient database confirmed that, based on the current trend of increase, it is projected that there will likely be 1 case of PAS for every 200 cesarean deliveries in the United States in 2025 [4]. The greatest risk of PAS is intraoperative catastrophic postpartum hemorrhage,

CONTACT Hongbo Qi qihongbocy@gmail.com Department of Obstetrics and Gynecology, Women and Children's Hospital of Chongqing Medical University, Chongqing 401147, China; Xinyang Yu yu.xinyang@cqmu.edu.cn Department of Obstetrics, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China.
*Xiafei Wu and Jie He are joint first authors.
**Hongbo Qi and Xinyang Yu are co-corresponding authors.

Supplemental data for this article can be accessed online at https://doi.org/10.1080/07853890.2024.2442065.

which can result in disseminated intravascular coagulation, local organ damage, and maternal mortality [5,6]. Therefore, the management of intraoperative bleeding in patients with PAS is crucial to reduce the occurrence of serious complications.

Endovascular interventional techniques are increasingly utilized during the perioperative phase to mitigate bleeding from aberrant placental implantation and reduce the rate of hysterectomy. Among these techniques, resuscitative endovascular balloon occlusion of the internal iliac artery, common iliac artery, abdominal aorta, and uterine artery are commonly adopted methods [7]. Notably, recent studies have underscored the superiority of abdominal aorta occlusion over iliac artery balloon occlusion in terms of recovery speed and reduced severe complications [8–10].

Despite these advancements, a subset of PAS patients does not derive the anticipated benefits from prophylactic resuscitative endovascular balloon occlusion of the aorta (REBOA). Such patients continue to experience severe intraoperative bleeding, necessitating extensive blood transfusions or even hysterectomy. While the current body of research has extensively explored the safety and efficacy of prophylactic arterial balloons, there remains a gap in understanding the specific patient factors that predispose to severe postpartum hemorrhage (SPPH) even after employing these interventions. Addressing this gap, our study endeavors to pinpoint the risk factors associated with SPPH in PAS patients undergoing elective cesarean delivery post-REBOA intervention.

Materials and methods

Ethics statement

This study adheres to the Declaration of Helsinki and was approval by the Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University on 2 September 2022 (Approval No: 2022-K416). As this research constitutes a retrospective case–control study, the ethics committee waived the requirement for participants' informed consent.

Study design and population

This retrospective case–control study was conducted at the First Affiliated Hospital of Chongqing Medical University. We reviewed patients diagnosed with PAS who underwent REBOA during cesarean delivery from January 2017 to December 2021. For the diagnosis of PAS, we followed the 2019 International Federation of Gynecology and Obstetrics (FIGO) classification standards [11]. Cases that underwent hysterectomy were diagnosed based on postoperative pathological findings. For the remaining patients, diagnosis relied on the clinical criteria combined with intraoperative observations. The decision to utilize prophylactic REBOA was informed by a prenatal ultrasound scoring system introduced in China in 2016, which evaluates PAS risk via cesarean history and eight ultrasound criteria [12,13]. Those who achieved a score of ≥8 were identified as high risk for severe complications and were thus considered for prophylactic REBOA placement. Exclusion criteria included: (1) incomplete clinical or follow-up data; (2) presentation of stillbirth; (3) multiple pregnancies; and (4) presence of either cardiovascular disease or a coagulation disorder. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Data collection

We retrospectively collected clinical information on demographics, previous medical history, pregnancy complications and perinatal management, and maternal and neonatal outcomes from the hospital information system. Baseline data included age, body mass index (BMI), and gestational age. The previous medical history covered gravidity, parity, and the number of cesarean deliveries. Pregnancy complications encompassed hypertensive disorders complicating pregnancy, gestational diabetes mellitus, and placenta previa. Perinatal management data consisted of prenatal ultrasound details, preoperative blood routine and coagulation tests, and intraoperative conditions. Maternal and neonatal outcomes included delivery-related complications, intervention-related complications, intensive care unit (ICU) admissions, postoperative hospitalization duration, birthweight, and Apgar scores.

Outcome definition

In this study, PAS patients undergoing cesarean delivery with REBOA were classified into two groups based on the occurrence of SPPH: those who developed SPPH (case group) and those without SPPH complications (control group). SPPH was defined by any of the following criteria: intraoperative blood loss of ≥1500 mL, transfusion of ≥4 units of packed red blood cells (PRBC), intraoperative hysterectomy, or sequential uterine artery embolization to manage bleeding. Intraoperative blood loss was measured using volumetric and/or

weighing methods, adjusted for amniotic fluid and irrigation.

Management of the patients

Patients with strong preoperative suspicion of PAS were managed in a planned manner, admitted 1–3 days before surgery, and underwent preoperative laboratory tests, blood preparation, and multidisciplinary consultation. On the day of the cesarean delivery, under local anesthesia and guided by angiographic fluoroscopy, a balloon catheter was placed in the infrarenal abdominal aorta, above the aortic bifurcation. After successful placement, patients were immediately transferred to the operating room. Upon arrival, epidural anesthesia was administered for cesarean delivery. Once the fetus was delivered and the umbilical cord clamped, the occlusion balloon was immediately inflated. Obstetricians then surgically excised the portions of the placenta closely adhered to the myometrium and subsequently reconstructed the uterus. If removal of the placental tissue was deemed unfeasible, an immediate hysterectomy was performed. If there was no active bleeding in the uterine region or within the pelvis, the balloon was deflated and extracted before closing the skin.

Statistical analyses

Statistical analysis was performed using R software (version 4.1.1, https://www.r-project.org/). Continuous variables were represented as Mean ± SD or Median (IQR), while categorical data were denoted by *n* (%). Independent sample *t*-tests or Mann–Whitney tests were used to compare continuous variables, and the chi-square test or Fisher's exact test was employed for categorical variables. All tests were two-sided, with $p < 0.05$ indicating statistical significance.

To mitigate bias, an analysis of covariance was conducted for all variables. The variance inflation factor (VIF) was used to assess multicollinearity, with a VIF >10 indicating severe covariance, resulting in the removal of redundant variables. Propensity score matching (PSM) was then applied to reduce selection bias. A 1:2 match ratio between the case and control groups was achieved using nearest neighbor matching with a caliper width of 0.02, without replacement.

Univariate logistic regression provided crude odds ratios (OR) with 95% confidence intervals (95% CI). Variables with $p < 0.1$ were included in a multivariate logistic regression analysis using the forward stepwise conditional method to calculate adjusted ORs (aOR). Based on the identified independent risk factors, a nomogram was developed. The diagnostic performance of the nomogram was evaluated using a receiver operating characteristic (ROC) curve, with cut-off points determined at the maximum Youden's index. Smooth curve fitting was performed to explore nonlinear relationships between risk factors and outcomes. Inflection points were identified using a recursive algorithm, followed by a segmented regression model for threshold effect analysis.

Results

Baseline and characteristic comparison

Among the 2890 PAS patients who underwent cesarean delivery, 447 were treated with REBOA based on the preoperative ultrasound score of 8 or higher. After excluding 23 patients for various reasons, 424 patients met the eligibility criteria for the study (Figure 1). Out of these, 102 developed SPPH despite the REBOA intervention (case group), while the remaining 322 did not exhibit SPPH (control group). Following PSM, the case group was narrowed down to 79 patients, and the control group to 130 patients. After PSM, no significant difference in baseline characteristics were observed between the two groups. The demographic and clinical characteristics of all patients are detailed in Table 1.

Compared to the control group, the case group had a significantly higher parity ($p = 0.032$) and a heightened incidence of placenta increta and percreta ($p < 0.001$). Preoperative laboratory tests revealed significant differences in erythrocyte count ($p = 0.001$), hemoglobin ($p = 0.003$), hematocrit ($p = 0.007$), prothrombin time ($p = 0.005$), fibrinogen ($p = 0.011$), fibrin degradation products ($p < 0.001$), and D-dimer ($p < 0.001$). Among the outcome characteristics, intraoperative blood loss, PRBC transfusion, uterine artery embolization, hysterectomy, intraoperative bladder injury, ICU admission, and inpatient days differed significantly between the two groups ($p < 0.001$). Newborns in the case group had a lower birthweight ($p = 0.022$), but Apgar scores were comparable between the groups. Furthermore, only two patients in the case group experienced venous thromboembolism, with no other intervention-related complications observed. After PSM, differences in parity ($p = 0.500$), birthweight ($p = 0.887$), and erythrocyte count ($p = 0.078$) were no longer statistically significant between the two groups.

In total, 28 factors related to the outcome were analyzed in this study. A multicollinearity analysis of covariates was performed, and variables with

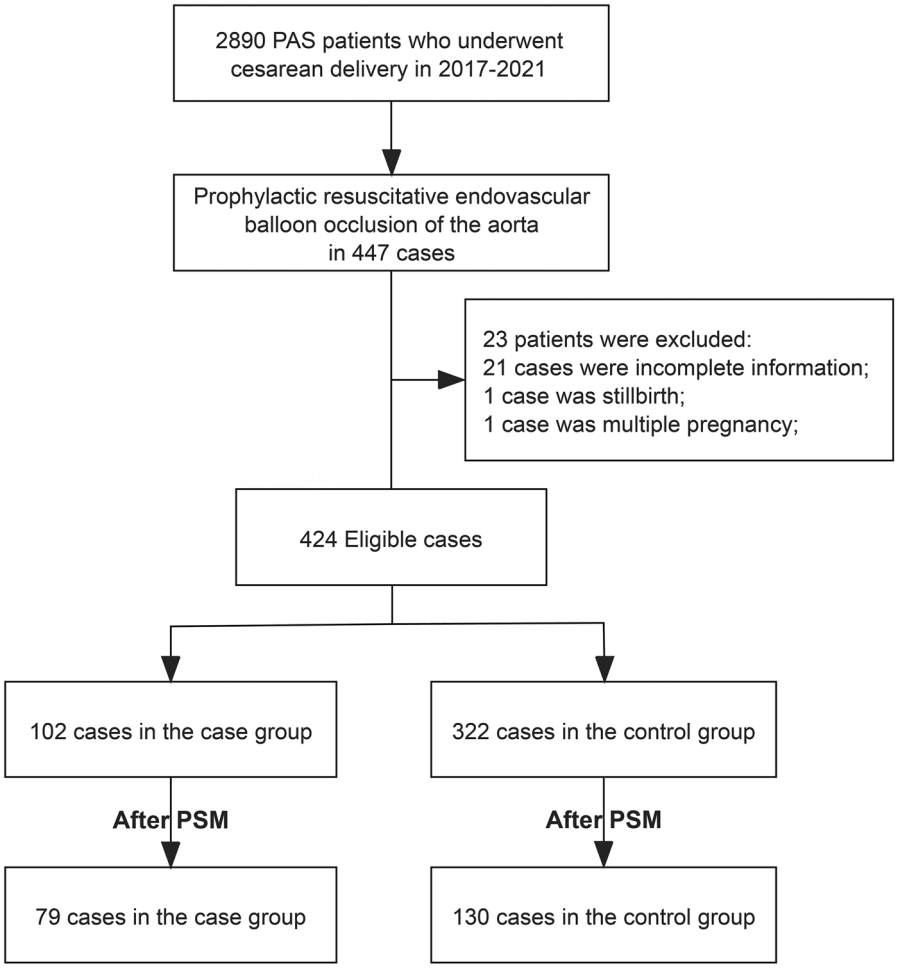

Figure 1. Research flow chart. PAS: placenta accreta spectrum; PSM: propensity score matching.

significant VIF values were excluded (Figure S1). As a result, hematocrit and fibrin degradation products were not included in the subsequent analyses.

Risk factors associated with outcomes

In all included populations, univariate logistic regression analysis revealed that patients with higher gravidity ($p = 0.060$), placenta increta ($p < 0.001$), and percreta ($p < 0.001$) had increased odds of experiencing SPPH. The risk of SPPH was found to increase with elevated prothrombin time ($p = 0.010$) and D-dimer levels ($p < 0.001$). Additionally, decreased levels of hemoglobin ($p = 0.010$) and fibrinogen ($p = 0.010$) were also associated with a heightened risk. In the PSM population, the presence of placenta increta (OR 2.91, 95% CI 1.50–5.69, $p < 0.001$), percreta (OR 24.10, 95% CI 8.44–87.79, $p < 0.001$), elevated prothrombin time (OR 1.66, 95% CI 1.16–2.41, $p = 0.010$), increased D-dimer levels (OR 1.46, 95% CI 1.23–1.77, $p < 0.001$), and decreased hemoglobin (OR 0.98, 95% CI 0.96–1, $p = 0.030$), and fibrinogen levels (OR 0.7, 95% CI 0.48–0.99, $p = 0.050$) were significant predictors of SPPH (Table 2).

To further eliminate potential impacts on outcomes, we performed multivariate logistic regression analyses, adjusting for potential confounders (Table 3). The case group was significantly associated with increta (aOR 2.69, 95% CI 1.53–7.74, $p = 0.001$), percreta (aOR 14.24, 95% CI 6.77–29.98, $p < 0.001$), hemoglobin levels (aOR 0.98, 95% CI 0.96–1, $p = 0.025$), and D-dimer levels (aOR 1.37, 95% CI 1.2–1.57, $p < 0.001$). After PSM, the depth of placenta invasion, hemoglobin levels (aOR 0.98, 95% CI 0.95–1, $p = 0.050$), and D-dimer levels (aOR 1.36, 95% CI 1.12–1.65, $p = 0.002$) remained significant independent predictors of SPPH. Notably, there were significant associations between the depth of placental invasion and risk (increta: aOR 3, 95% CI 1.49–6.03, $p = 0.002$; percreta: aOR 21.77, 95% CI 6.57–72.09, $p < 0.001$).

The independent risk factors identified by multivariate logistic regression in the PSM population were used to develop a nomogram (Figure 2). The clinical validity of this model was assessed, yielding an area under the curve of 0.80 (95% CI 0.73–0.86). With a cut-off value set at 0.41, the model demonstrated a sensitivity of 0.68 and a specificity of 0.84. The positive and

Table 1. Baseline characteristics of patients in the case and control groups.

	Before PSM			After PSM		
Characteristics	Case ($n=102$)	Control ($n=322$)	*P*-value	Case ($n=79$)	Control ($n=130$)	*P*-value
Age (years)	33 (7)	32 (6)	0.002	33 (6)[a]	32 (5)	0.449
BMI	21.8 (4.95)	21.5 (3.73)	0.134	21.5 (4.9)	21.4 (3.18)	0.634
Gestational age (days)	253 (9)	257 (9)	<0.001	256 (9)	256 (8.75)	0.809
Weight gain in pregnancy (kg)	12.5 (5.5)	13 (6)	0.301	13 (6)	13 (4.75)	0.615
Gravidity			0.081			0.661
1–3	28 (27.45)	121 (37.58)		26 (32.91)	48 (36.92)	
≥4	74 (72.55)	201 (62.42)		53 (67.09)	82 (63.08)	
Parity			0.032			0.500
0	4 (3.92)	7 (2.17)		3 (3.80)	4 (3.08)	
1	66 (64.71)	250 (77.64)		57 (72.15)	103 (79.23)	
≥2	32 (31.37)	65 (20.19)		19 (24.05)	23 (17.69)	
Previous cesarean delivery			0.217			0.782
0	4 (3.92)	14 (4.35)		3 (3.80)	7 (5.38)	
1	73 (71.57)	254 (78.88)		63 (79.75)	105 (80.77)	
≥2	25 (24.51)	54 (16.77)		13 (16.46)	18 (13.85)	
History of abortions	84 (82.35)	259 (80.43)	0.776	64 (81.01)	101 (77.69)	0.692
History of placenta previa	3 (2.94)	16 (4.97)	0.583	3 (3.80)	7 (5.38)	0.746
History of intrauterine operation	88 (86.3)	271 (84.2)	0.606	66 (83.5)	106 (81.5)	0.713
Complication						
IVF-ET	0 (0)	3 (0.93)	1.000	0 (0.00)	2 (1.54)	0.528
HDCP	2 (1.96)	6 (1.86)	1.000	1 (1.27)	4 (3.08)	0.652
GDM	21 (20.59)	51 (15.84)	0.336	13 (16.46)	23 (17.69)	0.968
Uterine fibroid	0 (0)	10 (3.1)	0.127	0 (0)	6 (4.6)	0.085
Complete placenta previa	96 (94.12)	290 (90.06)	0.293	73 (92.41)	117 (90.00)	0.735
Pernicious placenta previa	95 (93.14)	294 (91.30)	0.704	73 (92.41)	121 (93.08)	1.000
Symptoms of vaginal bleeding	45 (44.12)	133 (41.30)	0.699	32 (40.51)	54 (41.54)	0.998
Symptoms of abdominal pain	14 (13.7)	42 (13)	0.859	11 (13.9)	16 (12.3)	0.736
Placenta site			0.200			0.316
Anterior	12 (11.76)	59 (18.32)		8 (10.13)	23 (17.69)	
Posterior	43 (42.16)	140 (43.48)		35 (44.30)	55 (42.31)	
Anterior–posterior	47 (46.08)	123 (38.20)		36 (45.57)	52 (40.00)	
Depth of PAS			<0.001			<0.001
Accreta	33 (32.35)	223 (69.25)		24 (30.38)	89 (68.46)	
Increta	34 (33.33)	84 (26.09)		29 (36.71)	37 (28.46)	
Percreta	35 (34.31)	15 (4.66)		26 (32.91)	4 (3.08)	
Preoperative laboratory tests						
Erythrocyte count (10^{12}/L)	3.62 (0.64)	3.78 (0.56)	0.001	3.64 (0.69)	3.78 (0.51)	0.078
Hemoglobin (g/L)	110 (18)	115 (17)	0.003	111 (19)	115 (14)	0.017
Hematocrit (%)	33.7 (4.7)	34.7 (4.45)	0.007	33.7 (5.1)[a]	34.65 (3.75)	0.050
Platelet (10^9/L)	186 (72.75)	180.5 (74.75)	0.142	184 (66)	177.5 (65)	0.744
PT (s)	11.5 (1.28)	11.3 (1)	0.005	11.5 (1.2)	11.3 (0.88)	0.004
APTT (s)	27.25 (4.93)	26.4 (4.78)	0.404	27.3 (5.35)	26.15 (3.65)	0.065
TT (s)	15.85 (1)	15.8 (1.18)	0.818	15.8 (1.05)	15.9 (1)	0.649
Fibrinogen (g/L)	3.99 (1.33)	4.32 (1.12)	0.011	3.96 (1.26)[a]	4.33 (0.98)	0.047
FDP (μg/ml)	7 (6.1)	5.3 (3.73)	<0.001	7 (5.8)	5.45 (4.15)	<0.001
D-dimer (mg/L)	2.98 (2.84)	2.04 (1.62)	<0.001	3.1 (2.46)	2.08 (1.72)	<0.001
Pregnancy outcome						
Birthweight (g)	2702.5 (565)[a]	2847.5 (523)	0.022	2750 (510)[a]	2820 (560)	0.887
Apgar score						
1 min	8 (1)	9 (1)	0.125	9 (1)	9 (1)	0.795
5 min	10 (1)	10 (1)	0.229	10 (1)	10 (0.25)	0.750
10 min	10 (0)	10 (0)	0.109	10 (0)	10 (0)	0.838
Blood loss (mL)	2000 (1200)	600 (250)	<0.001	2000 (1100)	600 (200)	<0.001
PRBC transfusion (units)	4 (3.5)	0 (0)	<0.001	3 (2.5)	0 (0)	<0.001
Uterine artery embolization	16 (15.7)	0 (0)	<0.001	11 (13.9)	0 (0)	<0.001
Hysterectomy	24 (23.5)	0 (0)	<0.001	17 (21.5)	0 (0)	<0.001
Bladder injury	10 (9.8)	2 (0.6)	<0.001	8 (10.1)	0 (0)	<0.001
Venous thromboembolism	2 (2)	0 (0)	0.057	1 (1.3)	0 (0)	0.378
ICU admission	14 (13.7)	1 (0.3)	<0.001	10 (12.7)	0 (0)	<0.001
Inpatient days (days)	8 (3)	6 (2)	<0.001	7 (3)	6 (2)	<0.001

Note: Continuous data are represented as median (IQR). Categorical data are represented as *n* (%). Chi-square test or Fisher's exact test for categorical variables and *t*-test and Mann–Whitney *U* test for normally distributed and non-normally distributed continuous variables, respectively.

[a]The variables conform to a normal distribution.

Abbreviations: PSM: propensity score matching; BMI: body mass index; IVF-ET: *In vitro* fertilization and embryo transfer; HDCP: hypertensive disorders complicating pregnancy; GDM: gestational diabetes mellitus; PT: prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time; FDP, fibrin degradation products; PRBC: packed red blood cells; ICU: intensive care unit.

Table 2. Univariate binary logistic regression analysis before and after PSM.

	Before PSM		After PSM	
Variables	Crude OR (95% CI)	*P*-value	Crude OR (95% CI)	*P*-value
Weight gain in pregnancy (kg)	0.98 (0.93—1.02)	0.280	0.98 (0.92–1.05)	0.600
Gravidity				
1–3	Ref		Ref	
≥4	1.59 (0.98—2.63)	0.060	1.19 (0.66–2.17)	0.560
Parity				
0	Ref		Ref	
1	0.46 (0.14—1.81)	0.230	0.74 (0.16–3.85)	0.700
≥2	0.86 (0.24—3.49)	0.820	1.1 (0.22–6.17)	0.910
Previous cesarean delivery				
0	Ref		Ref	
1	1.01 (0.35–3.63)	0.990	1.4 (0.37–6.67)	0.630
≥2	1.62 (0.52–6.16)	0.430	1.69 (0.39–8.97)	0.500
History of abortions	1.14 (0.65–2.07)	0.670	1.23 (0.62–2.51)	0.570
History of placenta previa	0.58 (0.13–1.78)	0.390	0.69 (0.15–2.58)	0.600
History of intrauterine operation	1.18 (0.63–2.24)	0.606	1.15 (0.55–2.41)	0.713
Complication				
HDCP	1.05 (0.15–4.65)	0.950	0.4 (0.02–2.79)	0.420
GDM	1.38 (0.77–2.4)	0.270	0.92 (0.42–1.91)	0.820
Complete placenta previa	1.77 (0.77–4.8)	0.220	1.35 (0.51–3.99)	0.560
Pernicious placenta previa	1.29 (0.58–3.3)	0.560	0.9 (0.31–2.8)	0.860
Symptoms of vaginal bleeding	1.12 (0.71–1.76)	0.620	0.96 (0.54–1.69)	0.880
Symptoms of abdominal pain	1.06 (0.55–2.03)	0.859	1.15 (0.51–2.63)	0.736
Placenta site				
Anterior	Ref		Ref	
Posterior	1.51 (0.76–3.18)	0.250	1.83 (0.76–4.78)	0.190
Anterior–Posterior	1.88 (0.95–3.95)	0.080	1.99 (0.83–5.2)	0.140
Depth of PAS				
Accreta	Ref		Ref	
Increta	2.74 (1.59–4.71)	<0.001	2.91 (1.5–5.69)	<0.001
Percreta	15.77 (7.93–32.8)	<0.001	24.1 (8.44–87.79)	<0.001
Birthweight (g)	1 (1.0–1.0)	0.020	1 (1.0–1.0)	0.890
Preoperative laboratory tests				
Erythrocyte count (10^{12}/L)	1.01 (0.87–1.11)	0.910	1.06 (0.92–1.39)	0.450
Hemoglobin (g/L)	0.98 (0.96–0.99)	0.010	0.98 (0.96–1)	0.030
Platelet (10^9/L)	1 (1–1.01)	0.150	1 (1–1.01)	0.840
PT (s)	1.4 (1.09–1.81)	0.010	1.66 (1.16–2.41)	0.010
APTT (s)	1.02 (0.96–1.08)	0.570	1.07 (0.99–1.16)	0.100
TT (s)	0.95 (0.72–1.22)	0.690	0.9 (0.65–1.21)	0.510
Fibrinogen (g/L)	0.68 (0.52–0.89)	0.010	0.7 (0.48–0.99)	0.050
D-dimer (mg/L)	1.43 (1.27–1.63)	<0.001	1.46 (1.23–1.77)	<0.001

Abbreviations: HDCP: hypertensive disorders complicating pregnancy; GDM: gestational diabetes mellitus; PT: prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time.

Table 3. Multivariate logistic regression before and after PSM.

	Before PSM		After PSM	
Variables	Adjusted OR[a] (95% CI)	*P*-value	Adjusted OR[a] (95% CI)	*P*-value
Depth of PAS				
Accreta	Ref		Ref	
Increta	2.69 (1.53–4.74)	0.001	3 (1.49–6.03)	0.002
Percreta	14.24 (6.77–29.98)	<0.001	21.77 (6.57–72.09)	<0.001
Hemoglobin (g/L)	0.98 (0.96–1)	0.025	0.98 (0.95–1)	0.050
D-dimer (mg/L)	1.37 (1.2–1.57)	<0.001	1.36 (1.12–1.65)	0.002

[a]Adjusting for gravidity, prothrombin time, and fibrinogen.

negative predictive values were 0.80 and 0.77, respectively (Figure 3).

Threshold effect analysis

After adjusting for confounders, a potential nonlinear relationship between both hemoglobin and D-dimer levels and the outcome was observed, as depicted by the smooth curve fitting (Figure 4). The inflection points for hemoglobin and D-dimer in relation to the outcome were identified as 114 g/L and 6.22 mg/L, respectively. These points were determined using a segmented regression model and a recursive algorithm. The likelihood ratio test, comparing the segmented model to the original model, indicated no significant difference in the results ($p = 0.107$ for hemoglobin and $p = 0.412$ for D-dimer) (Table 4). Consequently, the nonlinear relationship between hemoglobin, D-dimer, and the outcome was not statistically significant, indicating no threshold effect.

Discussion

In this retrospective case–control study, we explored the relationship between specific risk factors and the incidence of SPPH in PAS patients treated with REBOA. Our primary analysis revealed that placenta increta, percreta, lower hemoglobin levels, and elevated

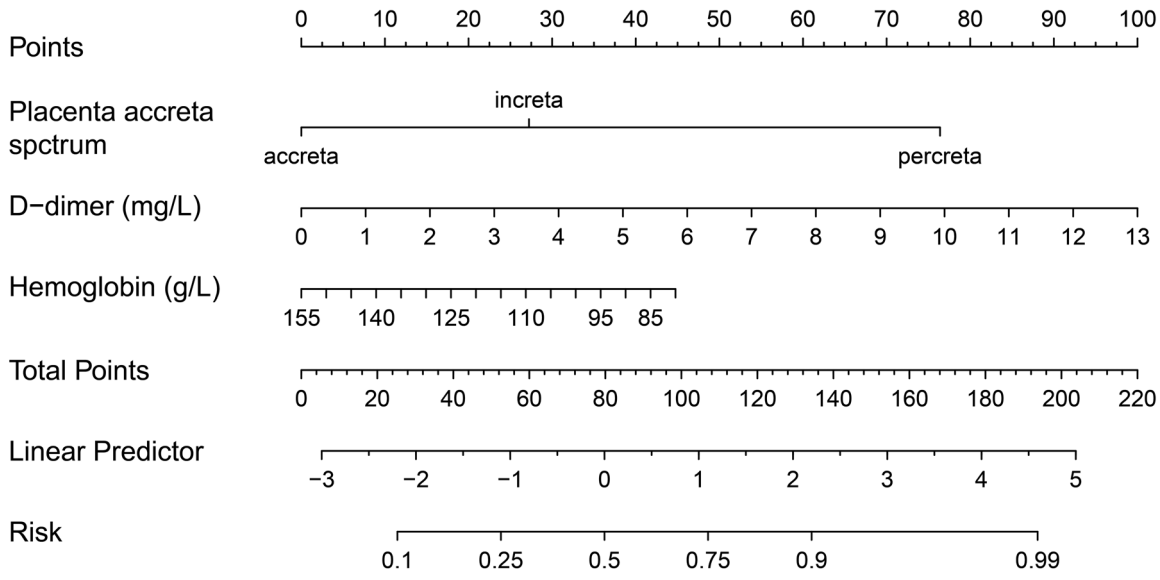

Figure 2. A nomogram was developed based on independent risk factors screened by multivariate logistic regression in the PSM population.

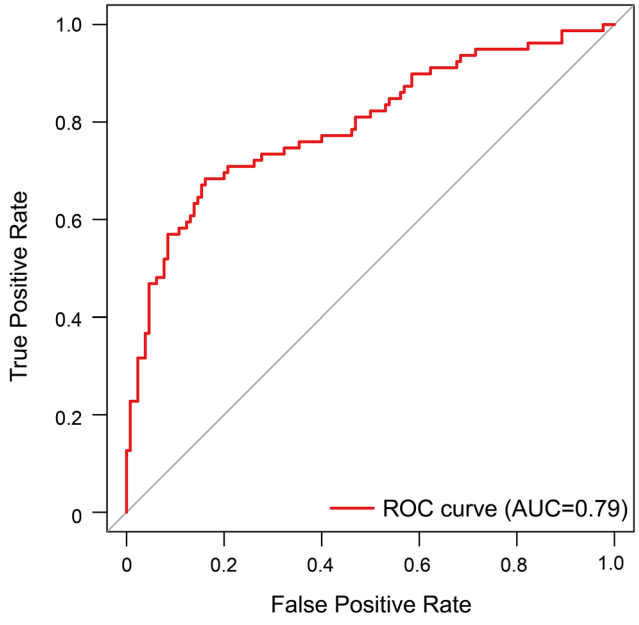

Figure 3. The ROC of the multivariate logistic regression model.

D-dimer levels significantly contribute to the risk of SPPH. This correlation underscores the importance of heightened vigilance and thorough preoperative assessment in patients exhibiting these characteristics.

Balloon occlusion of the abdominal aorta serves as a prophylactic technique providing critical proximal control of blood flow, effectively reducing the risk of hemorrhage by occluding collateral vessels to the uterus alongside the uterine artery and internal iliac artery. This approach has been validated as both safe and effective, complementing conservative surgical methods [7,8]. Notably, in our cohort of 424 PAS patients managed with REBOA, the rate of hysterectomy was remarkably low, with only 24 patients requiring this intervention, markedly below historically reported rates for PAS management [14–16]. Furthermore, the incidence of catheter-related complications was minimal, with only two cases of venous thromboembolism observed. These outcomes highlight the potential of REBOA to reduce the need for severe surgical interventions and associated complications. However, it's important to acknowledge that a subset of patients still faced challenges, including SPPH or hysterectomy, despite the advantages offered by REBOA.

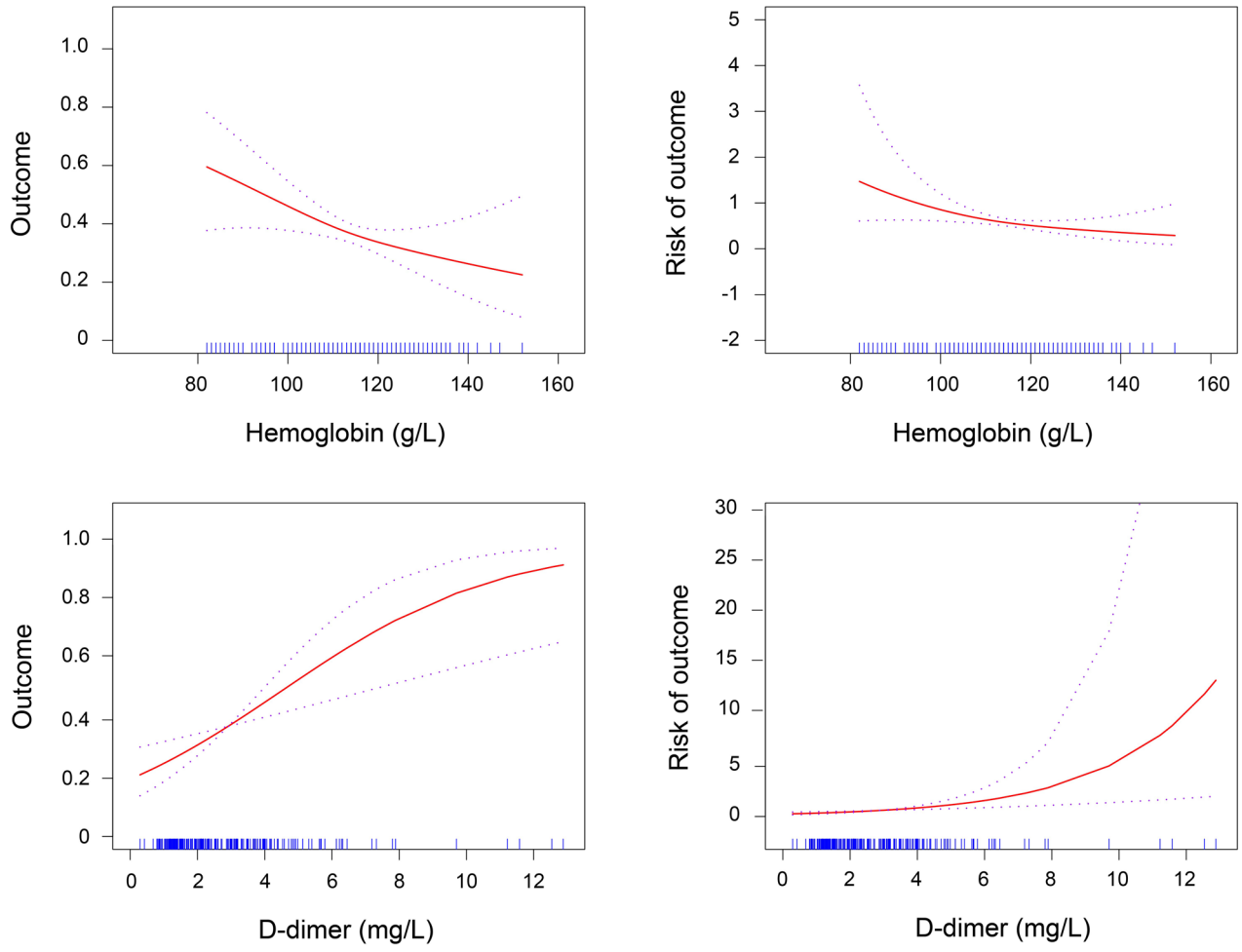

Figure 4. Relationship between hemoglobin and D-dimer levels with SPPH post-REBOA in PAS patients. After adjusting for the depth of PAS, hemoglobin, and D-dimer, a nonlinear relationship was observed between the levels of hemoglobin and D-dimer and the outcome.

Table 4. Threshold effects analysis of preoperative hemoglobin and D-dimer values on outcomes using piecewise linear regression.

	Hemoglobin (g/L)		D-dimer (mg/L)	
Outcomes	Odds ratio[a] (95% CI)	*P*-value	Odds ratio[a] (95% CI)	*P*-value
Infection point	114		6.22	
< Infection point	0.95 (0.91–0.99)	0.014	1.29 (1.02–1.64)	0.035
≥ Infection point	1.01 (0.96–1.06)	0.702	1.93 (0.67–5.51)	0.222
LR test		0.107		0.412

[a]Adjusted: depth of PAS, hemoglobin, D-dimer.
Abbreviation: LR test: Likelihood ratio test.

The management of abnormally invasive placenta, especially in case of increta and percreta, presents significant clinical challenges. Previous research has shown that these conditions are associated with a higher incidence of severe maternal morbidity compared to placenta accreta, They are more prone to severe intraoperative bleeding (≥5000 ml), frequent large intraoperative transfusions (PRBC ≥10 units), higher hysterectomy rates, and an increased risk of surgical mortality [4,17–19]. Consistent with their findings, our study indicated that patients with abnormally invasive placenta, especially those with percreta, faced challenges in achieving optimal intraoperative hemorrhage control and were more susceptible to severe delivery-related complications, even with early REBOA management. These findings highlight the critical importance of advanced surgical planning and the potential role of REBOA in mitigating intraoperative blood loss.

Optimizing preoperative hemoglobin levels emerges as a pivotal strategy for mitigating morbidity in PAS patients [20]. While there is no direct evidence suggesting that prenatal optimization of hemoglobin is specifically recommended for PAS cases, prior studies on postpartum hemorrhage have indicated that women with hemoglobin levels <90 g/L at delivery face an elevated risk of excessive blood loss both during delivery and in the immediate postpartum period [21]. The International Society for Abnormally

Invasive Placenta (IS-AIP) guidelines recommend maintaining hemoglobin levels >110 g/L prior to 28 weeks of gestation and >105 g/L after 28 weeks of gestation [22]. Our findings align with existing literature, suggesting that maintaining preoperative hemoglobin levels above certain thresholds may significantly reduce the risk of major transfusions. While our data also manifested a potential nonlinear relationship with an inflection point at 114 g/L, this observation was not statistically significant. These results underscore the value of preoperative interventions, including iron supplementation and blood management, as integral components of PAS care.

Furthermore, our analysis emphasizes the prognostic value of coagulation markers, particularly D-dimer, in predicting the severity of PAS and subsequent blood loss. Guo et al. [23] conducted an analysis on the coagulation test of 95 patients with a confirmed pathological diagnosis of PAS within 2 weeks prior to delivery. Their findings revealed that preoperative coagulation markers, notably prothrombin time, D-dimer, and fibrin degradation products, were associated with the severity of PAS and the volume of intraoperative blood loss. Elevated D-dimer levels, indicative of increased fibrinolysis activity, were significantly associated with adverse outcomes, suggesting that these markers could serve as crucial indicators for preoperative risk stratification and personalized management plans.

Our research highlights the profound significance of identifying and managing a specific subgroup of PAS patients who are at high risk for severe complications. By employing PSM, we were able to effectively reduce confounding factors, lending greater validity to our findings. This study deepens our comprehension of the complex risks tied to PAS and demonstrates the significant role of REBOA in addressing these challenges. We advocate for an integrated, multidisciplinary approach in preoperative planning that includes comprehensive risk assessments and customized management strategies, aiming to enhance the prognosis for PAS patients.

Nevertheless, our study also has some limitations. Firstly, we identified four adverse outcomes associated with the occurrence of SPPH. Given the varying definitions of SPPH across studies, this might introduce discrepancies when comparing our findings with those of other researchers. Secondly, due to the limited sample size at a single center, we were unable to analyze certain risk factors considered to be associated with PAS, such as adenomyosis, endometriosis, uterine anomalies, and ovarian disease, which may impact the generalizability of our findings. Moving forward, future efforts will focus on conducting a multicenter study to address these concerns and conducting a stratified analysis based on different pregnancy outcomes.

Conclusions

In conclusion, our study demonstrates that even with prophylactic REBOA, certain PAS patients remain at high risk for SPPH. Specifically, those identified as high risk through a prenatal ultrasound scoring system, and presenting with placenta increta, percreta, lower hemoglobin, and elevated D-dimer levels, are more likely to experience SPPH. These insights emphasize the need for targeted preoperative optimization and highlight the predictive importance of coagulation markers in managing PAS patients effectively.

Acknowledgments

We are grateful for the support from the '111 program' of Ministry of Education P.R.C and State Administration of Foreign Experts Affairs P.R.C. We would also like to express our gratitude to Jing Zeng for polishing the language of this article.

Author contributions

XFW and JH designed this project and completed the original draft. XFW, JH, YXB, and YQ G were involved in the data curation and statistical analysis. YXB and YQG interpreted the results. HBX, HBQ, and XYY provided guidance on the paper and revised the final version. HB Q and XY Y were the guarantor of this article.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

HBQ and XYY provided financial support. This work was supported by the National Key Research and Development Program of China (No. 2022YFC2704500) and Chongqing Yuzhong District Basic Research and Frontier Exploration Project (No. 20180108).

ORCID

Xiafei Wu http://orcid.org/0000-0003-2503-1383
Jie He http://orcid.org/0000-0002-2577-9247
Yuxiang Bai http://orcid.org/0009-0007-5243-6294
Yanqiong Gan http://orcid.org/0000-0002-8549-5510
Hongbing Xu http://orcid.org/0000-0003-2851-0793
Hongbo Qi http://orcid.org/0000-0003-3776-0487
Xinyang Yu http://orcid.org/0000-0002-3341-0183

Data availability statement

The data presented in this study are available on request from the corresponding author.

References

[1] Jauniaux E, Collins S, Burton GJ. Placenta accreta spectrum: pathophysiology and evidence-based anatomy for prenatal ultrasound imaging. Am J Obstet Gynecol. 2018;218(1):75–87. doi: 10.1016/j.ajog.2017.05.067.

[2] McKeogh RP, D'Errico E. Placenta accreta: clinical manifestations and conservative management. N Engl J Med. 1951;245(5):159–165. doi: 10.1056/NEJM195108022450501.

[3] Jauniaux E, Bunce C, Grønbeck L, et al. Prevalence and main outcomes of placenta accreta spectrum: a systematic review and meta-analysis. Am J Obstet Gynecol. 2019;221(3):208–218. doi: 10.1016/j.ajog.2019.01.233.

[4] Matsuzaki S, Mandelbaum RS, Sangara RN, et al. Trends, characteristics, and outcomes of placenta accreta spectrum: a national study in the United States. Am J Obstet Gynecol. 2021;225(5):534.e1–534.e38. doi: 10.1016/j.ajog.2021.04.233.

[5] Fonseca A, Ayres De Campos D. Maternal morbidity and mortality due to placenta accreta spectrum disorders. Best Pract Res Clin Obstet Gynaecol. 2021;72:84–91. doi: 10.1016/j.bpobgyn.2020.07.011.

[6] Wang Y, Zhou Y, Zeng L, et al. Analysis of risk factors for massive intraoperative bleeding in patients with placenta accreta spectrum. BMC Pregnancy Childb. 2022;22(1):116.

[7] Hawthorn BR, Ratnam LA. Role of interventional radiology in placenta accreta spectrum (PAS) disorders. Best Pract Res Clin Obstet Gynaecol. 2021;72:25–37. doi: 10.1016/j.bpobgyn.2021.01.007.

[8] Shahin Y, Pang CL. Endovascular interventional modalities for haemorrhage control in abnormal placental implantation deliveries: a systematic review and meta-analysis. Eur Radiol. 2018;28(7):2713–2726. doi: 10.1007/s00330-017-5222-0.

[9] Li K, Zou Y, Sun J, et al. Prophylactic balloon occlusion of internal iliac arteries, common iliac arteries and infrarenal abdominal aorta in pregnancies complicated by placenta accreta: a retrospective cohort study. Eur Radiol. 2018;28(12):4959–4967. doi: 10.1007/s00330-018-5527-7.

[10] Dai M, Zhang F, Li K, et al. The effect of prophylactic balloon occlusion in patients with placenta accreta spectrum: a Bayesian network meta-analysis. Eur Radiol. 2022;32(5):3297–3308. doi: 10.1007/s00330-021-08423-6.

[11] Jauniaux E, Ayres-de-Campos D, Langhoff-Roos J, et al. FIGO classification for the clinical diagnosis of placenta accreta spectrum disorders. Int J Gynaecol Obstet. 2019;146(1):20–24. doi: 10.1002/ijgo.12761.

[12] Zhong Y, Zhang A, Wang Y, et al. Value of ultrasonic scoring system for predicting risks of placenta accreta. Chin J Perinat Med. 2016;19(9):705–709.

[13] Chong Y, Zhang A, Wang Y, et al. An ultrasonic scoring system to predict the prognosis of placenta accreta: a prospective cohort study. Medicine (Baltimore). 2018;97(35):e12111. doi: 10.1097/MD.0000000000012111.

[14] Bodelon C, Bernabe-Ortiz A, Schiff MA, et al. Factors associated with peripartum hysterectomy. Obstet Gynecol. 2009;114(4):927. doi: 10.1097/AOG.0b013e3181ba039c.

[15] Jin R, Guo Y, Chen Y. Risk factors associated with emergency peripartum hysterectomy. Chin Med J-Peking. 2014;127(5):900–904. doi: 10.3760/cma.j.issn.0366-6999.20132023.

[16] Jauniaux E, Chantraine F, Silver RM, et al. FIGO consensus guidelines on placenta accreta spectrum disorders: epidemiology. Int J Gynaecol Obstet. 2018;140(3):265–273. doi: 10.1002/ijgo.12407.

[17] Marcellin L, Delorme P, Bonnet MP, et al. Placenta percreta is associated with more frequent severe maternal morbidity than placenta accreta. Am J Obstet Gynecol. 2018;219(2):193.e1–193.e9. doi: 10.1016/j.ajog.2018.04.049.

[18] Maison N, Rattanaburi A, Pruksanusak N, et al. Intraoperative blood volume loss according to gestational age at delivery among pregnant women with placenta accreta spectrum (PAS): an 11-year experience in Songklanagarind Hospital. J Obstet Gynaecol. 2022;42(3):424–429. doi: 10.1080/01443615.2021.1910638.

[19] Gulino FA, Guardo FD, Zambrotta E, et al. Placenta accreta and balloon catheterization: the experience of a single center and an update of latest evidence of literature. Arch Gynecol Obstet. 2018;298(1):83–88. doi: 10.1007/s00404-018-4780-y.

[20] Allen L, Jauniaux E, Hobson S, et al. FIGO consensus guidelines on placenta accreta spectrum disorders: nonconservative surgical management. Int J Gynaecol Obstet. 2018;140(3):281–290. doi: 10.1002/ijgo.12409.

[21] Kavle JA, Stoltzfus RJ, Witter F, et al. Association between anaemia during pregnancy and blood loss at and after delivery among women with vaginal births in Pemba Island, Zanzibar, Tanzania. J Health Popul Nutr. 2008;26(2):232–240.

[22] Collins SL, Alemdar B, van Beekhuizen HJ, et al. Evidence-based guidelines for the management of abnormally invasive placenta: recommendations from the International Society for Abnormally Invasive Placenta. Am J Obstet Gynecol. 2019;220(6):511–526. doi: 10.1016/j.ajog.2019.02.054.

[23] Guo Z, Han X, Zhang H, et al. Association between pre-delivery coagulation indicators and invasive placenta accreta spectrum. Clin Appl Thromb Hemost. 2022;28:1146444017. doi: 10.1177/10760296211070580.